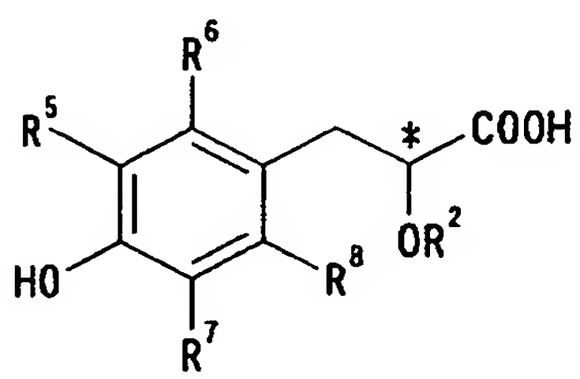
Claims

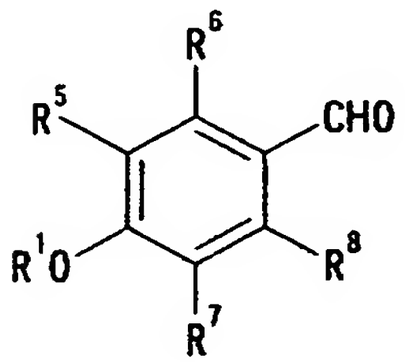
1. A process for producing an optically active 3-(4-hydroxyphenyl)propionic acid of the formula (6):



(6)

wherein R^2 is an alkyl group, R^5 to R^8 are each independently a hydrogen atom or a substituent; and the symbol * is a chiral carbon atom,

or a salt thereof, which comprises reacting a benzaldehyde of the formula (1):



(1)

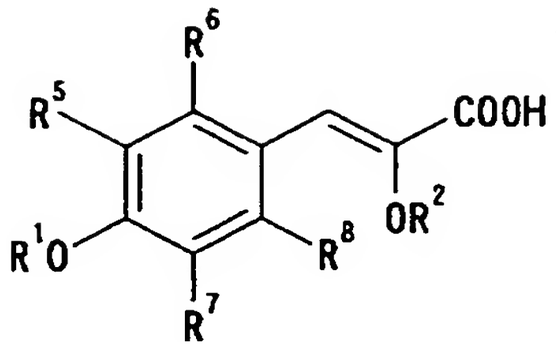
wherein R^1 is a protective group; and R^5 to R^8 are each the same as defined above,

with a glycolic acid derivative of the formula (2):

(2)

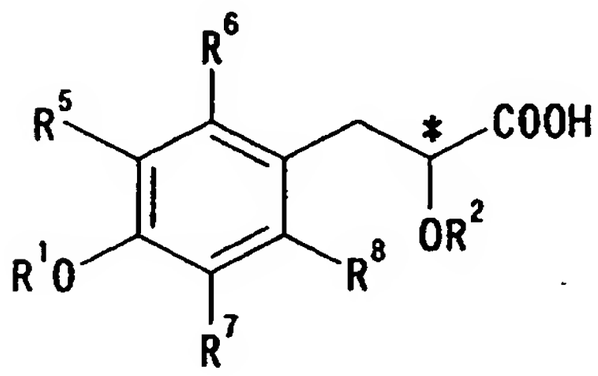
wherein R^3 is a hydrocarbon group, and R^2 is the same as defined above,

hydrolyzing the resulting product to give a cinnamic acid of the formula (4):



(4)

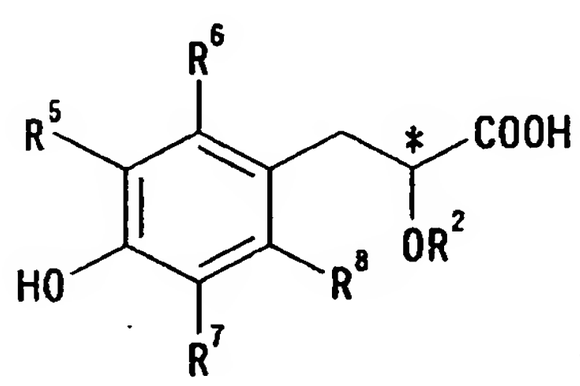
wherein R^1, R^2, and R^5 to R^8 are each the same as defined above, or a salt thereof, and subjecting the cinnamic acid (4) or a salt thereof to asymmetric hydrogenation to give an optically active phenylpropionic acid of the formula (5):



(5)

wherein all the symbols are each the same as defined above, or a salt thereof, followed by deprotection.

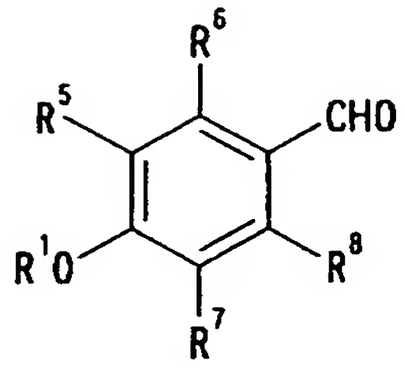
2. A process for producing an optically active 3-(4-hydroxyphenyl)propionic acid of the formula (6):



(6)

wherein R^2 is an alkyl group; R^5 to R^8 are each independently a hydrogen atom or a substituent; and the symbol * is a chiral carbon atom,

or a salt thereof, which comprises reacting a benzaldehyde of the formula (1):



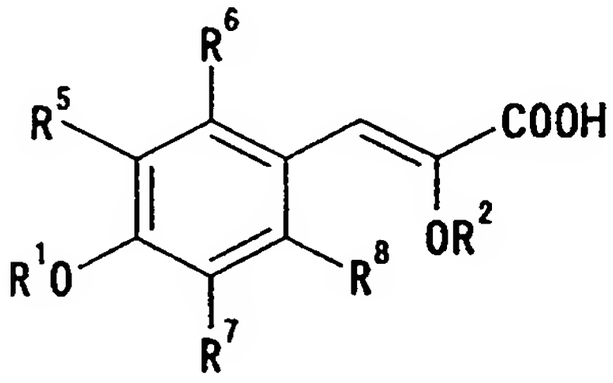
(1)

wherein R^1 is a protective group; and R^5 to R^8 are each the same as defined above,

with a glycolic acid derivative of the formula (2):

(2)

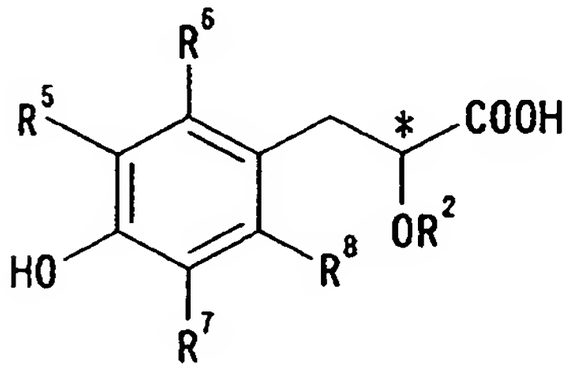
wherein R^3 is a hydrocarbon group, and R^2 is the same as defined above, followed by hydrolysis to give a cinnamic acid of the formula (4):



(4)

wherein R^1, R^2, and R^5 to R^8 are each the same as defined above, or a salt thereof, and subjecting the cinnamic acid (4) or a salt thereof to asymmetric hydrogenation.

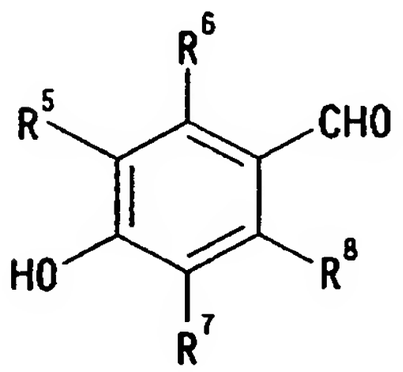
3. A process for producing an optically active 3-(4-hydroxyphenyl)propionic acid of the formula (6):



(6)

wherein R^2 is an alkyl group; R^5 to R^8 are each independently a hydrogen atom or a substituent; and the symbol * is a chiral carbon atom,

or a salt thereof, which comprises reacting a 4-hydroxybenzaldehyde of the formula (7):

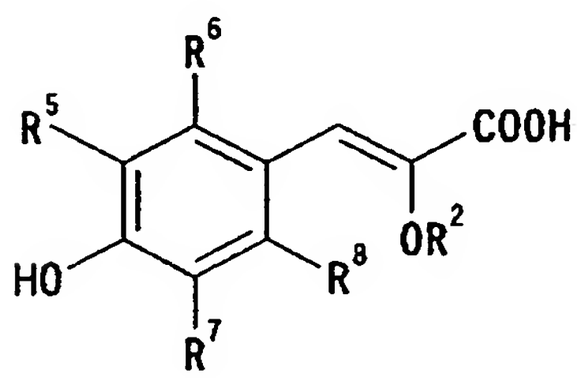


(7)

wherein R^5 to R^8 are each the same as defined above, with a glycolic acid derivative of the formula (2):

(2)

wherein R^3 is a hydrocarbon group; and R^2 is the same as defined above, followed by hydrolysis to give a 4-hydroxycinnamic acid of the formula (9):



(9)

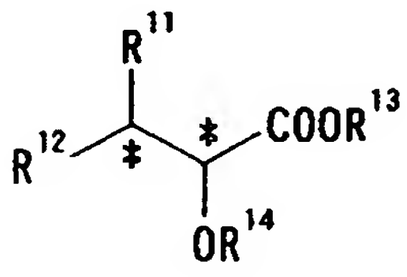
wherein R^2, and R^5 to R^8 are each the same as defined above, or a salt thereof, and subjecting the 4-hydroxycinnamic acid (9) or a salt thereof to asymmetric hydrogenation.

4. The process according to any one of claims 1 to 3, wherein the asymmetric hydrogenation is carried out in the presence of a chiral catalyst.

5. The process according to any one of claims 1 to 4, wherein the chiral catalyst is a transition metal complex.

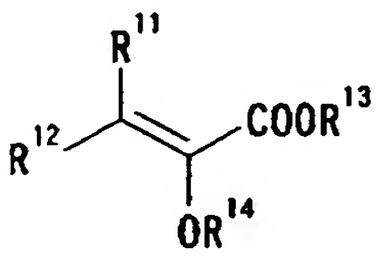
6. The process according to claim 5, wherein the transition metal complex is a complex of the metal of Groups 8 to 10 in the periodic table.

7. A process for producing an optically active carboxylic acid of the formula (12):



(12)

wherein R^{11} and R^{12} are each independently a hydrogen atom or a substituent; R^{13} is a hydrogen atom, an optionally substituted hydrocarbon group or a metal atom; R^{14} is a hydrogen atom or a protective group; and the symbol * is an chiral carbon atom, or a salt thereof, which comprises subjecting an α,β-unsaturated carboxylic acid of the formula (11):



(11)

wherein R^{11} to R^{14} are each the same as defined above, or a salt thereof, to asymmetric hydrogenation in the presence of a transition metal complex, provided that when the transition metal complex is rhodium, the protective group represented by R^{14} in the above formula (11) is a group other than acyl.

8. The process according to claim 7, wherein the transition metal complex is a complex of the metal of Groups 8 to 10 in the periodic table.

9. The process according to claim 1 or 3, wherein the chiral catalyst is a mixture of a chiral ligand and a transition metal compound.

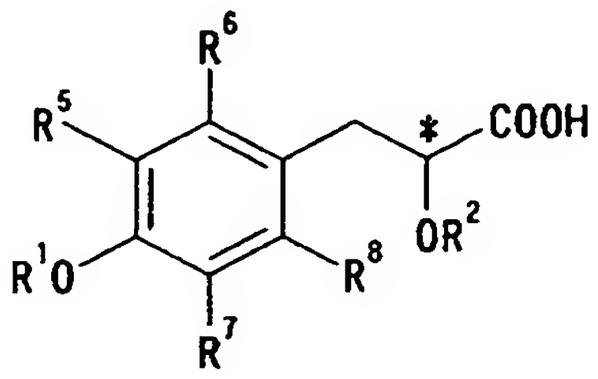
10. The process according to any one of claims 1 to 3, wherein the optically active phenylpropionic acid of the formula (5) or a salt thereof obtained by the method according to any one of claims 1 to 3 is crystallized from a solvent.

11. The process according to claim 10, wherein the solvent used for the crystallization is a member selected from the group consisting of hydrocarbons, alcohols, ketones and water, and a mixture thereof.

12. The process according to any one of claims 1 to 3, wherein the optically active 3-(4-hydroxyphenyl)propionic acid of the formula (6) or a salt thereof obtained by the method according to any one of claims 1 to 3 is crystallized from a solvent.

13. The process according to claim 12, wherein the solvent used for the crystallization is a member selected from the group consisting of aromatic hydrocarbons, aliphatic hydrocarbons, alcohols and water, and a mixture thereof.

14. A process for producing an optically active phenylpropionic acid of the formula (5):

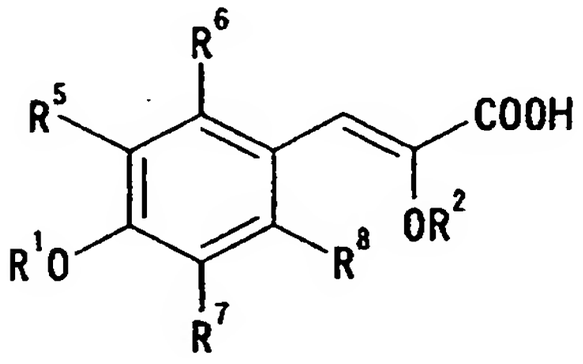


(5)

wherein R^1 is a protective group; R^2 is an alkyl group; R^5 to R^8 are each independently a hydrogen atom or a substituent; and the symbol * is an chiral carbon atom,

or a salt thereof

which comprises subjecting a cinnamic acid of the formula (4):



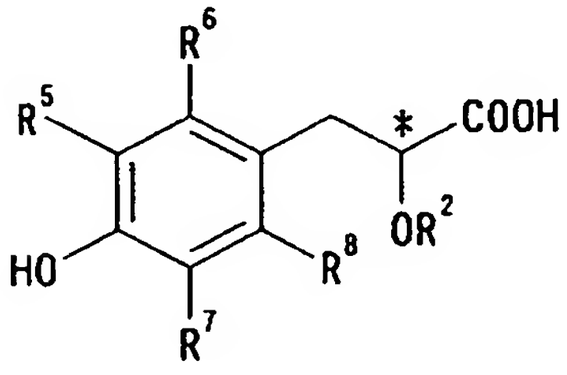
(4)

wherein R^1, R^2, and R^5 to R^8 are each the same as defined above,

or a salt thereof,

to asymmetric hydrogenation.

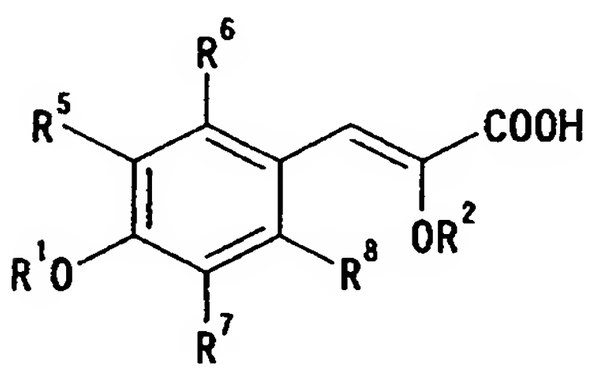
15. A process for producing an optically active 3-(4-hydroxyphenyl)propionic acid of the formula (6):



(6)

wherein R^2 is an alkyl group; R^5 to R^8 are each independently a hydrogen atom or a substituent; and the symbol * is a chiral carbon atom,

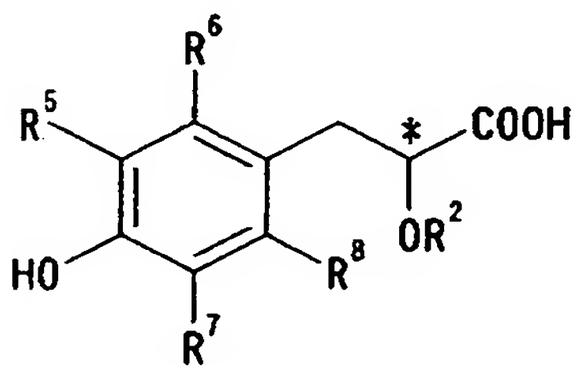
or a salt thereof, which comprises subjecting a cinnamic acid of the formula (4):



(4)

wherein R^1, R^2, and R^5 to R^8 are each the same as defined above, or a salt thereof, to asymmetric hydrogenation.

16. A process for producing an optically active 3-(4-hydroxyphenyl)propionic acid of the formula (6):

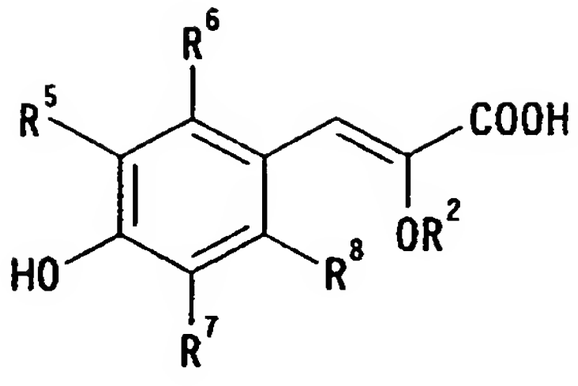


(6)

wherein R^2 is an alkyl group; R^5 to R^8 are each independently a hydrogen atom or a substituent; and the symbol * is a chiral carbon atom,

or a salt thereof,

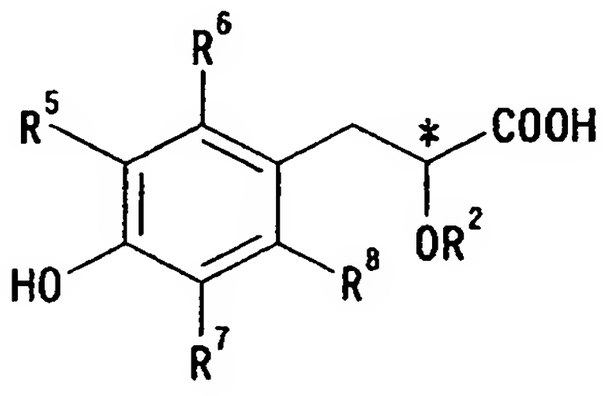
which comprises subjecting a 4-hydroxycinnamic acid of the formula (9):



(9)

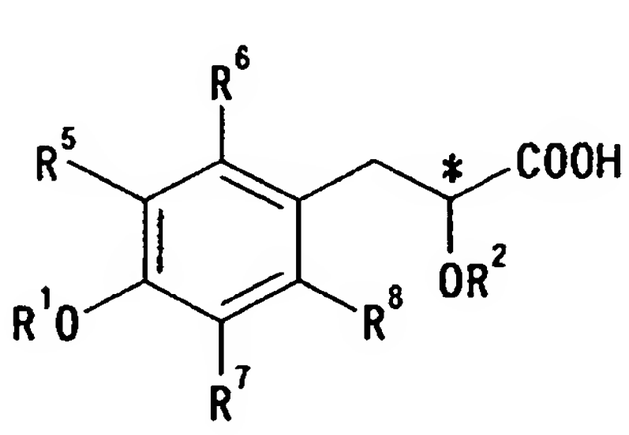
wherein R^2, and R^5 to R^8 are each the same as defined above, or a salt thereof to asymmetric hydrogenation.

17. A process for producing an optically active 3-(4-hydroxyphenyl)propionic acid of the formula (6):



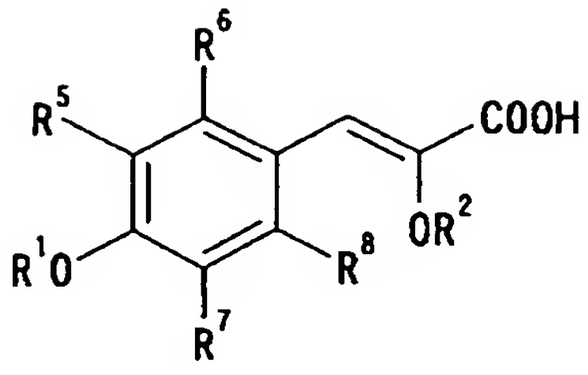
(6)

wherein R^2 is an alkyl group; R^5 to R^8 are each independently a hydrogen atom or a substituent; and the symbol * is a chiral carbon atom,
or a salt thereof, and an optically active phenylpropionic acid of the formula (5):



(5)

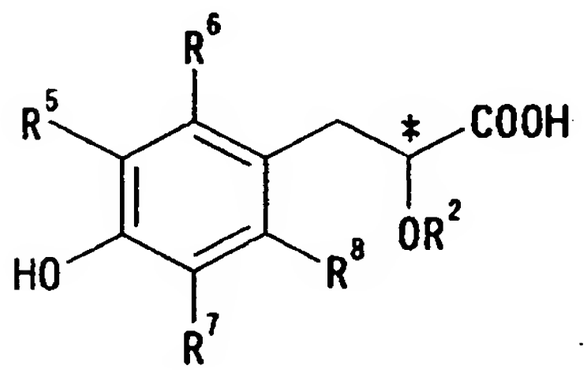
wherein R^1 is a protective group; and R^2, R^5 to R^8 and the symbol * are each the same as defined above,
or a salt thereof, which comprises subjecting a cinnamic acid of the formula (4):



(4)

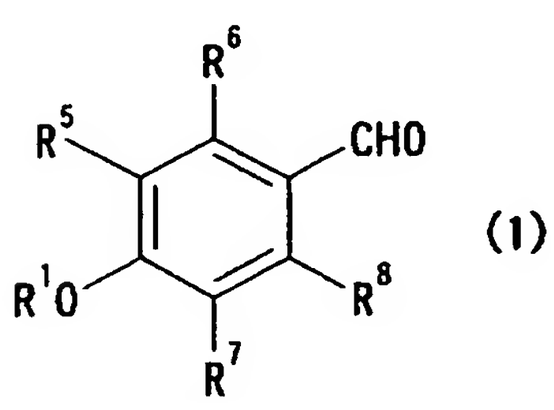
wherein R^1, R^2, and R^5 to R^8 are each the same as defined above, or a salt thereof, to asymmetric hydrogenation.

18. A process for producing an optically active 3-(4-hydroxyphenyl)propionic acid of the formula (6):



(6)

wherein R^2 is an alkyl group, R^5 to R^8 are each independently a hydrogen atom or a substituent; and the symbol * is a chiral carbon atom,
or a salt thereof, which comprises reacting a benzaldehyde of the formula (1):



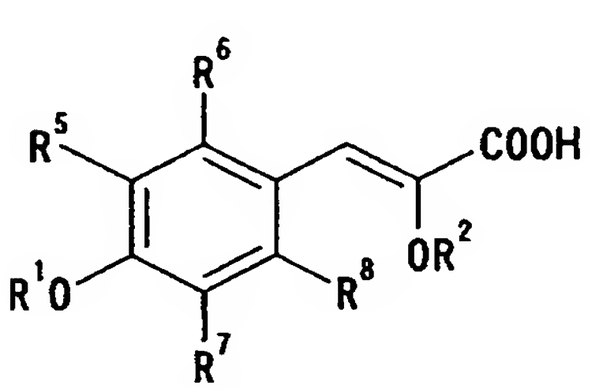
(1)

wherein R^1 is a protective group; and R^5 to R^8 are each the same as defined above,
with a glycolic acid derivative of the formula (2):

(2)

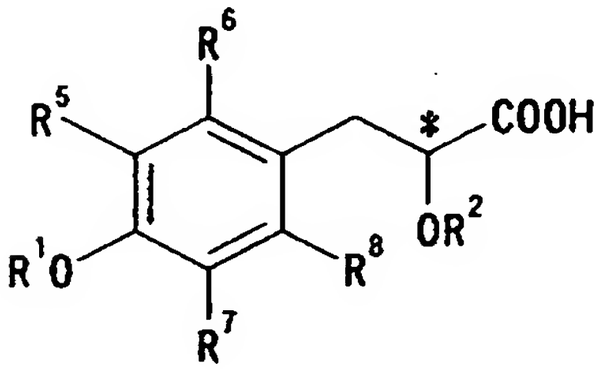
wherein R^3 is a hydrocarbon group, and R^2 is the same as defined above,

hydrolyzing the resulting product to give a cinnamic acid of the formula (4):



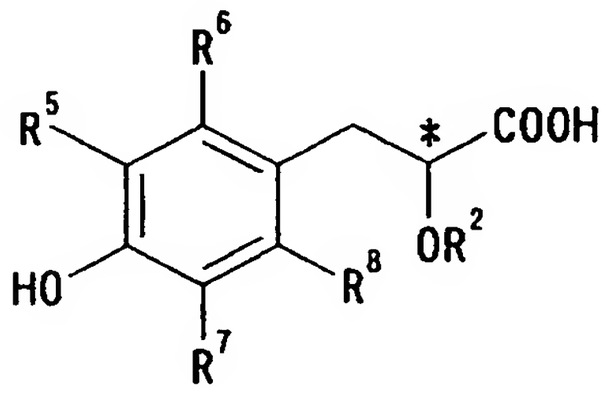
(4)

wherein R^1, R^2, and R^5 to R^8 are each the same as defined above, or a salt thereof, and subjecting the cinnamic acid (4) or a salt thereof to asymmetric hydrogenation to give an optically active phenylpropionic acid of the formula (5):



(5)

wherein all the symbols are each the same as defined above, or a salt thereof, and an optically active 3-(4-hydroxyphenyl)propionic acid of the formula (6):

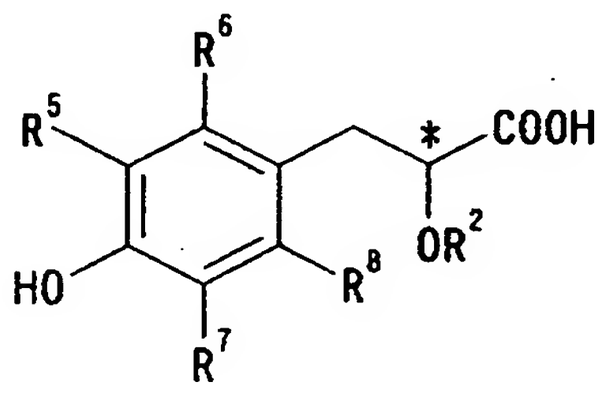


(6)

wherein all the symbols are each the same as defined above, or a salt thereof, followed by deprotection.

Abstract

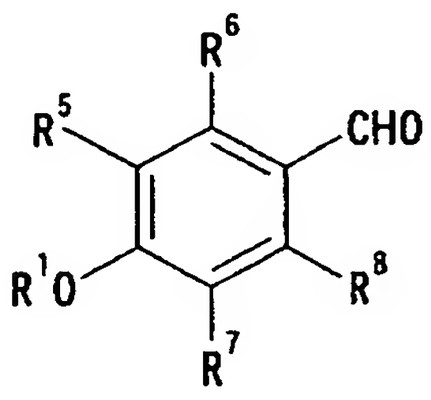
The present invention relates to a process for producing an optically active 3-(4-hydroxyphenyl)propionic acid useful as intermediates for medicines, through short steps in good yield and with high optical purity. More specifically, the present invention relates to a process for producing an optically active 3-(4-hydroxyphenyl)propionic acid of the formula (6):



(6)

wherein R^2 is an alkyl group; R^5 to R^8 are each independently a hydrogen atom or a substituent; and the symbol * is an chiral carbon atom,

or a salt thereof, which comprises reacting a benzaldehyde of the formula (1):



(1)

wherein R^1 is a protective group; and R^5 to R^8 are each the same as defined above,

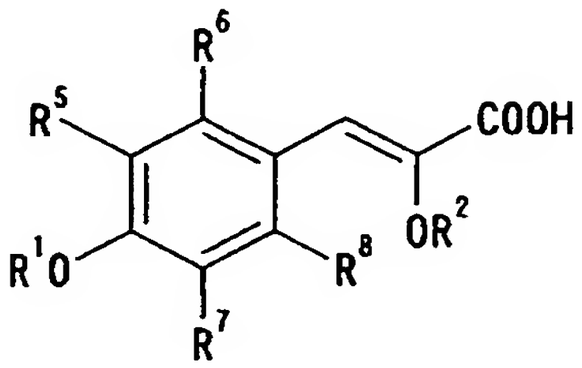
with a glycolic acid derivative of the formula (2):

(2)

wherein R^3 is a hydrocarbon group; and R^2 is the same as defined

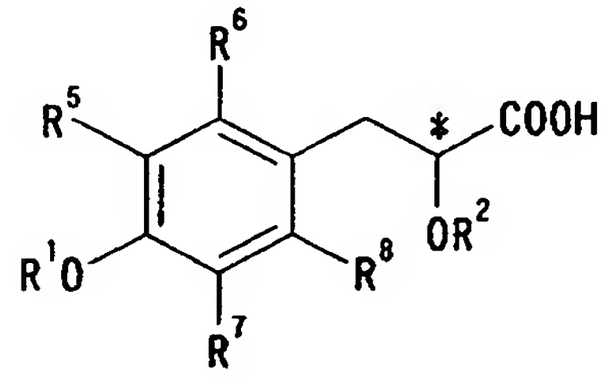
above,

hydrolyzing the resulting product to give a cinnamic acid of the formula (4):



(4)

wherein R^1, R^2 and R^5 to R^8 are each the same as defined above, or a salt thereof, and subjecting the resulting cinnamic acid (4) or a salt thereof to asymmetric hydrogenation to give an optically active phenylpropionic acid of the formula (5):



(5)

wherein all the symbols are each the same as defined above, or a salt thereof, followed by deprotection.